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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,725	KANAZAWA ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *4,5 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-17 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 21 Apr 2008, in which claims 11, 12, 14, 20 and 22 have been amended to changes the breadth and scope of the claim; and claims 2-9, 11-15 and 18-22 have been amended to clarify the meaning of the claim.

This application is the national stage entry of PCT/JP05/01801, filed 08 Feb 2005; and claims benefit of foreign priority document JAPAN 2004-032329, filed 09 Feb 2004.

Claims 1-22 are pending in the current application. Claim 18, drawn to a non-elected invention, are withdrawn. Claims 4 and 5, drawn to a non-elected species, are withdrawn.

Objections Withdrawn

Applicant's Amendment, filed 21 Apr 2008, with respect to objections to the specification has been fully considered and is persuasive, as the informalities identified have been corrected.

This objection has been **withdrawn**.

Applicant's Amendment and Remarks, filed 21 Apr 2008, with respect to objections to claims 2-3, 6-9, 11-17 and 19-22 has been fully considered and is persuasive, as the informalities identified in claims 2-3, 6-9, 11-15 and 19-22 have been

corrected and remarks regarding claims 16 and 17 not containing informalities are persuasive.

This objection has been **withdrawn**.

Rejections Withdrawn

Applicant's Amendment, filed 21 Apr 2008, with respect to rejection of claims 12, 14, 20 and 22 under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as the claims as amended do not equate treatment of a diseases with treatment of a symptom of said disease.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 21 Apr 2008, with respect to rejection of claims 11-14 and 19-22 under 35 U.S.C. 112, first paragraph, as not reasonably providing enablement for prophylaxis of metabolic syndrome and said symptoms has been fully considered and is persuasive, as the claims as amended do not recite a pharmaceutical composition capable of preventing metabolic syndrome and said symptoms.

This rejection has been **withdrawn**.

The following rejections are reiterated and maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-17 and 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussolari et al. (US Patent Application Publication US 2003/0045553, published 6 Mar 2003, cited in PTO-892).

Bussolari et al. discloses a composition for administering one or more glucose readsorption inhibitor and one or more PPAR modulator for the treatment of diabetes or Syndrome X, also known as metabolic syndrome (page 1, paragraph 12). Bussolari et al. discloses the specific PPAR modulator fenofibrate (page 8, paragraphs 104 and 129), addressing instant claims 2, 3 and 10. Bussolari et al. discloses the specific α-glucosidase inhibitor voglibose (page 10, paragraph 212 and 219), addressing instant claims 6, 7 and 10. Bussolari et al. discloses a pharmaceutical composition comprising one or more glucose readsorption inhibitor and one or more PPAR modulator (page 12, paragraph 303), addressing instant claims 1 and 15. Bussolari et al. discloses the

combination has the advantage of reducing the amount of either drug necessary, thereby reducing one or more adverse side-effects (page 12, paragraph 301), addressing instant claim 17. Bussolari et al. discloses the method of preparing the pharmaceutical composition comprising mixing the active ingredients (page 14, paragraph 323, lines 3-12), addressing instant claim 16. Bussolari et al. discloses the intended use of treating diabetes, Syndrome X, or associated symptoms (page 1, paragraph 12), where Syndrome X and associate symptoms include diabetes, IGT, IFG hyperinsulemia, insulin resistance, dyslipidemia, hypertension, and obesity. (page 1, paragraph 6), addressing the intended use disclosed in instant claims 11-14 and 19-22. Bussolari et al. discloses that "Optimal dosages to be administered may be readily determined by those skilled in the art, and will vary with the particular compound used, the strength of the preparation, the mode of administration, and the advancement of the disease condition. In addition, factors associated with the particular patient being treated, including patient age, weight, diet and time of administration, will result in the need to adjust dosages." (page 14, paragraph 328). Bussolari et al. discloses the combination of MCC-555, a PPAR modulator, at 3-30 mg/kg and T-1095, a glucose readsorption inhibitor, at 3-100 mg/kg (page 17, paragraph 344, lines 4-6), obviating the ratio of 3 mg/kg glucose readsorption inhibitor to 30 mg/kg PPAR modulator or the ratio of 10 parts be weight voglibose, a glucose readsorption inhibitor, to 100 parts by weight fenofibrate, a PPAR modulator, addressing instant claims 8 and 9.

Bussolari et al. does not specifically disclose the combination of fenofibrate and voglibose.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Bussolari et al. as the specific combination of fenofibrate and voglibose. Bussolari et al. discloses a pharmaceutical composition comprising one or more glucose readsorption inhibitor and one or more PPAR modulator (page 12, paragraph 303). Bussolari et al. discloses the specific α-glucosidase inhibitor voglibose (page 10, paragraph 212 and 219). An α-glucosidase catalyzes the hydrolysis of terminal, non-reducing 1,4-linked α-D-glucose residues with release of α-D-glucose. Inhibition of α-glucosidase would reduce the amount of glucose present to be readsorbed, and therefore inhibit glucose readsorption. Therefore the action of the α-glucosidase inhibitor voglibose results in an inhibition of glucose readsorption, and voglibose is a glucose readsorption inhibitor. Bussolari et al. discloses the specific PPAR modulator fenofibrate (page 8, paragraphs 104 and 129). It would have been simple substitution of one known element for another to obtain predictable results to use the glucose readsorption inhibitor voglibose and the PPAR modulator fenofibrate. Therefore a pharmaceutical composition of the specific combination of the PPAR modulator fenofibrate and the glucose readsorption inhibitor voglibose, would have been obvious to one of ordinary skill in the art at the time of the invention.

Response to Applicant's Remarks:

Applicant's Amendment and Remarks, filed 21 Apr 2008, have been fully considered about found not to be persuasive.

Applicant asserts that it is not *prima facie* obvious to substitute glucose readsorption inhibitors, such as the preferred embodiment of an SGLT inhibitor disclosed by Bussolari, with an α-glucosidase inhibitor because the mechanism of action is different. However, the invention of Bussolari is drawn to treatment of diabetes and Syndrome X (page 1, paragraph 2), with the SGLT inhibitor discloses as a preferred embodiment of a glucose readsorption inhibitor. As evidenced by Van Gaal et al. (Diabetologia, 2003, 46, pM44-M50, cited in PTO-892), agents for controlling postprandial glucose, agents for controlling fasting plasma glucose, and their use in combination therapy are known in the prior art for the same purpose of treating Type 2 diabetes (page M45, left column, paragraphs 1-4).

Applicant asserts that unexpected advantages are shown by the combination of fenofibrate and voglibose. However, the only evidence to support such an assertion, summarized in Table 1 on page 38 of the specification, is not clear and convincing with regard to these unexpected advantages. The data show an apparent decrease in mean GLU concentration for group 7 (Voglibose + Fenofibrate), from 4.83 ± 0.25 g/L before loading to 4.28 ± 0.37 g/L after loading. This contrasts to an apparent increase for group 4 (Voglibose), from 4.30 ± 0.47 g/L before loading to 4.50 ± 0.42 g/L after loading, and for group 5 (Fenofibrate), from 4.26 ± 0.55 g/L before loading to 4.78 ± 0.34 g/L after loading. However, this data is not clear and convincing because of the magnitude of the uncertainty of these measurements.

For example, if the GLU concentration before loading is high (mean + deviation) and after loading is low (mean - deviation), the following data are encompassed:

	GLU concentration before loading (g/L)	GLU concentration after loading (g/L)	GLU concentration change (g/L)
group 4 (Voglibose)	4.77	4.08	- 0.69
group 5 (Fenofibrate)	4.81	4.44	- 0.37
group 7 (Voglibose + Fenofibrate)	5.08	3.91	- 1.17

Given the evidence provided, the sum of the change for group 4 + group 5, -1.06, is approximately equal to the change for group 7, -1.17.

Further, there is sufficient overlap between the ranges of GLU concentration before and after loading for each group that it is possible that the same lack of change may have occurred in all of the groups, as illustrated in the table below:

	GLU concentration before loading (g/L)	GLU concentration after loading (g/L)	Overlap (g/L)
group 4 (Voglibose)	3.83-4.77	4.08-4.92	4.08-4.77
group 5 (Fenofibrate)	3.71-4.81	4.44-5.12	4.44-4.81
group 7 (Voglibose + Fenofibrate)	4.58-5.08	3.91-4.65	4.58-4.65

Therefore the provided data is not clear and convincing evidence of an unexpected advantage commensurate with the scope of the claims.

The following are new grounds of rejection necessitated by Applicant's Amendment, filed 21 Apr 2008, in which claims 11, 12, 14, 20 and 22 have been amended to changes the breadth and scope of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Amended Claims 12, 14, 20 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Amended Claims 12 and 20 recite "an agent for the treatment of at least one symptom selected from the group consisting of hyperlipemia, a symptom of diabetes, diabetes complications, a symptom of hyperglycemia after a meal in diabetics, impaired glucose tolerance (IGT), decrease of glucose tolerance, a symptom of hypertension, hyperinsulinemia, hyperammonemia, obesity or a complication thereof, fatty liver, and a symptom of hepatitis." Claims 14 and 22 recite "an agent for the treatment of at least one symptom selected from the group consisting of a symptom of diabetes, diabetes complications and a symptom of hyperglycemia after a meal in diabetics."

A symptom is a phenomenon that arises from and accompanies a particular disease or disorder and serves as an indication of it. However a symptom, for example the symptom of diabetes of thirst, may accompany many different diseases and disorders. Thus while a symptom may serve as an indication of a disease or disorder, many symptoms are not necessarily characteristic of a single disease or disorder, but may indicate the possible presence of a number of distinct diseases and disorders. The term "symptom of diabetes" renders the claim indefinite because a "symptom of diabetes" does not necessarily require a symptom that accompanies diabetes but includes a symptom accompanying a different disease or disorder that happens to be also be a symptom of diabetes, such as the symptom of thirst. This indefiniteness as to

what treatments are pointed out and claimed mean one of skill in the art would not be reasonably apprised of the metes and bounds of the claim.

One recommendation for definite language is "an agent for the treatment of at least one disease or condition selected from the group consisting of hyperlipemia, diabetes...", as this language particularly points out and distinctly claims what diseases or conditions said agent is for the treatment of.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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